

44. A method according to claim 41, wherein, in the presence of a  $Mn^{2+}$  cofactor, said thermostable ligase has a 12 fold higher fidelity than wild-type *Thermus thermophilus* ligase, when sealing a ligation junction between a pair of oligonucleotide probes hybridized to a target sequence where there is a mismatch with the oligonucleotide probe having its 3' end abutting the ligation junction at the base immediately adjacent to the ligation junction.

45. A method according to claim 42, wherein the thermostable ligase has an arginine adjacent its active site lysine in the KXDG motif where X is any amino acid.

46. A method according to claim 41, wherein the thermostable ligase has a molecular weight of 78 to 81 kDa as determined by SDS-PAGE.

47. A method according to claim 41, wherein the thermostable ligase has an amino acid sequence of SEQ. ID. No. 1.

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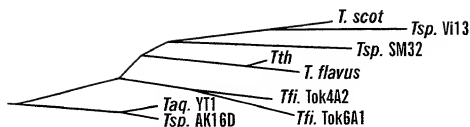


FIG. 1A

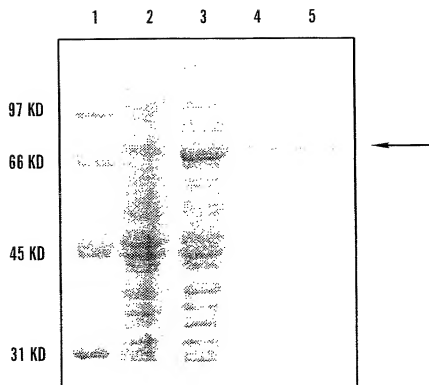
113 YTV	VERKVDGLSVNLYYE	129.....	231 LEE ...	TG 239.....	285 PFEADGVVVKLD	296 Tsp. AK16D
YTV	EHKVDGLSVNLYYE	.....	LEE ...	TG	.....	Taq. YTI
YTV	EHKVDGLSVNLYYE	.....	LEE	VEREG	.....	Tth
YTV	EHKVDGLSVNLYYE	.....	LEE	VEREG	.....	T. flavus
YTV	EHKVDGLSVNLYYE	.....	LEE ...	SG	.....	Tfi. Tok4A2
YTV	EHKVDGLSVNLYYE	.....	LEE ...	SG	.....	Tfi. Tok6A1
YTV	EHKVDGLSVNLYYE	.....	LEE ...	SG	.....	Tsp. SM32
YTV	EHKVDGLSVNLYYE	.....	LEE ...	SG	.....	Tsp. Vli3
YTV	EHKVDGLSVNLYYE	.....	LEE ...	SG	.....	T. scot

FIG. 1B

MTLEE	ARRRVNELRDLIRYHNYLYVLDAP	EISDAEYDRLLRELKEERFPELKSPD	60
TEQVG	ARPLEATFRPVRHPTRMYSLDNA	PSLDEVRAFEERIERALGRKGFPLYTV	120
GLSVN	LYYEEGILVFGATRGDGTGEEVTQ	NLLTIPTIPRRLTGVPDRLEVRGEV	180
AFRLN	QEEAAGERIPKNPRNAAAGSLRQ	KDPRVTARRGLRATFYALGLGEET	240
HDLL	LWLRRGFPVEHGFTRALGAEVVE	VYQAWLKERRKLPFEADGVVVKLD	300
LGYT	ARTPRPALAYKFFAEKEKTRLLS	VAFQVGRTRITPVGVLEPVFIEG	360
NESF	IEELDVRI GDWLVHKAGGVIPEV	LRVLKERRTGEEKPIIWPENCPEC	420
KVHR	CNPPLCPAKRFEAIRHYASKAMDI	QGLGEKLEKLEKGLVRDVADLYR	480
VNLER	MGEKSAENLLRQIEESKGRGLER	LLYALGLPGVGEVLARNLALRFG	540
LEDL	LEVEGVGELTARAILNTLKDPE	FRDLVRLKEAGVEMEAKEREGEAL	600
ELSR	PREEVKALLRRLGAKVTD	SVSRKTSFLVGVNGENPGSKLEK	660
IEERT	GKDPRALTA		674

FIG. 1C

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**FIG. 2**